REMARKS/ARGUMENTS

An Advisory Action has received on this application dated March 3, 2004, declining to enter the Amendment dated October 22, 2003 on the basis that the proposed amendment recites new issues that would require further consideration and/or search.

In this regard, the Examiner indicated that the proposed claims raised new issues under 35 USC 112, second paragraph. Claim 4 has been further amended.

The Examiner further checked the box that applicants reply had overcome certain rejections, but no details were given. Accordingly, the applicants below address the various issues raised by the Examiner in the Office Action of May 23, 2003.

In the Final Action of May 23, 2003, the Examiner rejected claims 1 to 4, 8 to 12, 16 and 23 under 35 USC 112, first paragraph, on the basis that the specification, while enabling for the use of Bacillus Calmette-Guerin (BCG) for the therapeutic treatment of condylomata acuminata, does not reasonably provide enablement for the use of all *Mycobacterium* species/strains for the therapeutic treatment of all disease conditions caused by papilloma virus infections.

It is noted that all claims are limited to the use of BCG. Claims 1 and 16 have been further amended to recite that the disease condition caused by papilloma virus is condylomata acuminata. Claims 2 and 3 have consequentially been deleted.

It is submitted that, having regard to the amendments made to the claims and the Examiner's comments with respect to enablement, claims 1 to 4, 8 to 12, 16 and 23, insofar as they remain in the application and in their amended form, are fully enabled by the disclosure and hence the rejection thereof under 35 USC 112, first paragraph, should be withdrawn.

The Examiner maintained rejection of claims 1 to 4 and 8 to 15 under 35 USC 112, second paragraph, as being vague and indefinite as lacking positive steps of the method.

While not agreeing with the Examiner since the features of subclaims 2 to 4 and 8 to 15, on the theory of claims differentiation, limit the recited treatment for the materials recited, these claims have been further amended to recite positive method steps.

Having regard thereto, it is submitted that claims 1 to 4 and 8 to 15, insofar as they remain in the application and in their amended form, no longer can be considered to be vague and indefinite in this respect, and hence the rejection thereof under 35 USC 112, second paragraph, should be withdrawn.

The Examiner maintained rejection of claims 1, 11 to 13 and 16 under 35 USC 112, second paragraph, as being rendered vague and indefinite by the use of the term "area of infection". While it believes the language to be clear on its face "area of" has been deleted from claims 1, 11 to 13 and 16.

Accordingly, it is submitted that these claims can no longer be considered to be rendered vague and indefinite and contrary to 35 USC 112, second paragraph in this respect and hence the rejection should be withdrawn.

The Examiner maintained rejection of claim 1 under 35 USC 112, second paragraph, as being rendered vague and indefinite by the use of the term "treatment dose". The term has been deleted from claim 1. Accordingly, it is submitted that claim 1 can no longer be considered to be contravene 35 USC 112, second paragraph, and hence the rejection should be withdrawn.

The Examiner maintained rejection of claim 8 under 35 USC 112, second paragraph, as being rendered vague and indefinite by the confusing language and in reciting method ranges that encompass the limitation of the claim.

The language of claim 8 has been amended in a manner, it is submitted, which removes any confusion which the Examiner considered to exist. It is clear from amended claim 8 that the method of claim 1 comprises applying BCG in 1 to 30 treatments using an individual treatment dosage of from 1 to 50 mg of BCG. The applications are each made at time intervals of 1 to 30 days for applications more than one.

Having regard thereto, it is submitted that claim 8 can no longer be considered to be vague and indefinite, and hence the rejection thereof under 35 USC 112, second paragraph, should be withdrawn.

The Examiner rejected claims 1, 2 and 9 under 35 USC 102(b) as being anticipated by Herr et al.

Applicants claims have been limited to the treatment of condylomata acuminata to which Herr et al makes no mention. Herr et al are concerned solely with the treatment of superficial bladder tumors.

Having regard to the limitations introduced to the claims, it is submitted that claims 1, 2 and 9, insofar as they remain in the application and in their amended form, are not anticipated by Herr et al and hence the rejection thereof under 35 USC 102(b) should be withdrawn.

The Examiner rejected claims 1 to 4, 8 to 16 and 20 to 23 under 35 USC 103(a) as being unpatentable over Herr et al in view of Morton. Reconsideration is requested having regard to the revisions made to the claims and the following discussion.

The present invention is directed to a method of treatment of the specific disease condition, condylomata acuminata, using BCG (claims 1, 4, 8 to 15), which, according to specific embodiments, may be formulated with a keratolytic agent, such as salicylic acid, as a cream for topical application to the infection. The present invention also is directed to a therapeutic composition for the treatment of

condylomata acuminata comprising BCG and a keratolytic agent for topical application to the infection (claims 16, 20 to 23).

It is submitted that a fair reading of the combination of cited prior art does not lead to the present invention as claimed. The Herr et al reference, as discussed above, is concerned with the treatment of superficial bladder cancers using BCG. There is no suggestion in Herr et al that BCG may be used for the treatment of any other disease condition. There is no suggestion whatsoever that BCG might be an effective treatment for condylomata acuminata.

Morton et al describe topical pharmaceutical compositions, which may be in gel or ointment form, which comprise a keratolytic agent, which may be salicylic acid, and a non-specific nucleoside analog, specifically idoxuridine, which are pro-drugs which apparently are activated by thymidine kinases (see page 1, lines 7 to 15). Thus, the active agent in the composition in Morton are pro-drugs. No other form of therapeutically-active material is suggested.

The Morton et al reference discloses that three non-specific nucleoside analogs have been suggested for the treatment of anogenital warts (condylomata acuminata) (page 1, lines 17 to 18). The purpose of the presence of the keratolytic agent in Morton is to cause thymidine kinases to be released in or around the affected tissue (page 1, lines 30 to 32). The composition of Morton may be used in the treatment of anogenital warts (page 2, line 17).

It is submitted that the combination of prior art does not disclose or suggest the invention. Herr et al disclose the use of BCG in the treatment of superficial bladder cancer. The treatment procedure involved intravesical administration of BCG (page 23, right hand column "Treatment Protocols"). Herr et al disclose no treatment using BCG other than to treat superficial bladder cancer nor any mode of treatment other than intravesical infection. There is no suggestion whatsoever that BCG might be useful to treat an entirely different disease condition (condylomata acuminata), preferably by topical application, particularly in the form of a cream.

Morton et al discloses treatment of condylomata acuminata but using an entirely different active ingredient, namely a non-specific nucleoside analogue, from BCG. The Morton reference discloses formulation of the active ingredient with a keratolytic agent, such as salicylic acid, which may be present in an amount of up to 15 wt% of the composition, and the formulation in the form of a gel or ointment for topical application. However, there is no suggestion whatsoever in Morton et al that BCG could be substituted for an entirely different active ingredient, namely a non-specific nucleoside analog, and still obtain an effective treatment for condylomata acuminata.

The Examiner states in the Final Action that:

> "Since the use of creams/gels/ointments is commonly used to deliver a therapeutic composition to a treatment site it would have been obvious to one of skill in the art to use the BCG, as disclosed by Herr et al., in a salicylic acid-containing topical cream/gel/ointment as disclosed by Morton in order to take advantage of the benefits of using a topical cream/gel (i.e. therapeutic composition adheres to area to be treated)".

It is not entirely clear that a topical application is a suitable mode of administration of BCG for superficial bladder cancer, especially in the absence of any suggestion in Herr that other than intravesical infection may be used.

The Examiner goes on to state:

> "One would expect the resulting composition to be an effective treatment for condylomata acuminata (warts) since BCG has been demonstrated to be an effective treatment for papillomas, (as disclosed by Herr et al), which also has human papilloma virus as a causative agent."

Putting aside the dispute between applicant and Examiner with respect to the interpretation to be placed on the Westenend et al reference, it is submitted that the present invention is concerned with technology which is known to be highly unpredictable. The Examiner questioned the enablement of applicants specification with respect to the treatment of disease condition caused by HPV generally and applicants claims have been limited to the treatment of condylomata acuminata.

It is submitted that there would be no expectation by a person skilled in the art that, if the BCG of Herr et al, would be formulated with the Morton et al composition, substituting for the non-specific, anti-viral nucleoside analog utilized in Morton for the treatment of anogental warts, the resulting composition would be effective in the treatment of condylomata acuminata, because:

- Herr et al teach only treatment of superficial bladder tumors with BCG

- Morton teach only treatment of condylomata acuminata by a non-specific, anti-viral nucleoside analog.

- There is no motivation in either document to make the urged substitution.

Accordingly, it is submitted that claims 1 to 4, 8 to 16 and 20 to 23 are patentable over the applied art and hence the rejection thereof under 35 USC 103(a) as being unpatentable over Herr et al in view of Morton, should be withdrawn.

It is believed that this application is now in condition for allowance and early and favourable consideration and allowance are respectfully solicited.

Respectfully submitted,

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